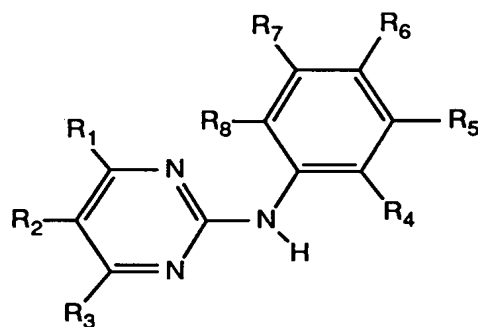


What is claimed is:

1. An N-phenyl-2-pyrimidine-amine compound of formula I



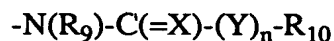
(I),

wherein

R<sub>1</sub> is 4-pyrazinyl, 1-methyl-1H-pyrrolyl, amino- or amino-lower alkyl-substituted phenyl wherein the amino group in each case is free, alkylated or acylated, 1H-indolyl or 1H-imidazolyl bonded at a five-membered ring carbon atom, or unsubstituted or lower alkyl-substituted pyridyl bonded at a ring carbon atom and unsubstituted or substituted at the nitrogen atom by oxygen,

R<sub>2</sub> and R<sub>3</sub> are each independently of the other hydrogen or lower alkyl,

one or two of the radicals R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are each nitro, fluoro-substituted lower alkoxy or a radical of formula II



(II),

wherein

R<sub>9</sub> is hydrogen or lower alkyl,

X is oxo, thio, imino, N-lower alkyl-imino, hydroximino or O-lower alkyl-hydrox-imino,

Y is oxygen or the group NH,

n is 0 or 1 and

R<sub>10</sub> is an aliphatic radical having at least 5 carbon atoms, or an aromatic, aromatic-aliphatic, cycloaliphatic, cycloaliphatic-aliphatic, heterocyclic or heterocyclic-aliphatic radical,

and the remaining radicals R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are each independently of the others hydrogen, lower alkyl that is unsubstituted or substituted by free or alkylated amino,

44

piperazinyl, piperidinyl, pyrrolidinyl or by morpholinyl, or lower alkanoyl, trifluoromethyl, free, etherified or esterified hydroxy, free, alkylated or acylated amino or free or esterified carboxy,  
or a salt of such a compound having at least one salt-forming group.

2. A compound of formula I according to claim 1, wherein one or two of the radicals  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are each nitro or a radical of formula II wherein

$R_9$  is hydrogen or lower alkyl,

X is oxo, thio, imino, N-lower alkyl-imino, hydroximino or O-lower alkyl-hydroximino,

Y is oxygen or the group NH,

n is 0 or 1 and

$R_{10}$  is an aliphatic radical having at least 5 carbon atoms or an aromatic, aromatic-aliphatic, cycloaliphatic, cycloaliphatic-aliphatic, heterocyclic or heterocyclic-aliphatic radical,

and the remaining radicals  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are each independently of the others hydrogen, lower alkyl that is unsubstituted or substituted by free or alkylated amino, piperazinyl, piperidinyl, pyrrolidinyl or by morpholinyl, or lower alkanoyl, trifluoromethyl, free, etherified or esterified hydroxy, free, alkylated or acylated amino or free or esterified carboxy,

and the remaining substituents are as defined in claim 1,

or a salt of such a compound having at least one salt-forming group.

3. A compound of formula I according to claim 1, wherein

$R_1$  is 4-pyrazinyl, 1-methyl-1H-pyrrolyl, amino- or amino-lower alkyl-substituted phenyl wherein the amino group in each case is free, alkylated by one or two lower alkyl radicals or acylated by lower alkanoyl or by benzoyl, 1H-indolyl or 1H-imidazolyl bonded at a five-membered ring carbon atom, or unsubstituted or lower alkyl-substituted pyridyl bonded at a ring carbon atom and unsubstituted or substituted at the nitrogen atom by oxygen,

$R_2$  and  $R_3$  are each independently of the other hydrogen or lower alkyl,

one or two of the radicals  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are each nitro, fluoro-substituted lower alkoxy or a radical of formula II wherein

$R_9$  is hydrogen or lower alkyl,

X is oxo, thio, imino, N-lower alkyl-imino, hydroximino or O-lower alkyl-hydrox-

45

imino,  
Y is oxygen or the group NH,  
n is 0 or 1 and  
R<sub>10</sub> is an aliphatic hydrocarbon radical having 5-22 carbon atoms, a phenyl or naphthyl radical each of which is unsubstituted or substituted by cyano, lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, (4-methyl-piperazinyl)-lower alkyl, trifluoromethyl, hydroxy, lower alkoxy, lower alkanoyloxy, halogen, amino, lower alkylamino, di-lower alkylamino, lower alkanoylamino, benzoylamino, carboxy or by lower alkoxycarbonyl, or phenyl-lower alkyl wherein the phenyl radical is unsubstituted or substituted as indicated above, a cycloalkyl or cycloalkenyl radical having up to 30 carbon atoms, cycloalkyl-lower alkyl or cycloalkenyl-lower alkyl each having up to 30 carbon atoms in the cycloalkyl or cycloalkenyl moiety, a monocyclic radical having 5 or 6 ring members and 1-3 ring hetero atoms selected from nitrogen, oxygen and sulfur, to which radical one or two benzene radicals may be fused, or lower alkyl substituted by such a monocyclic radical,  
and the remaining radicals R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are each independently of the others hydrogen, lower alkyl that is unsubstituted or substituted by amino, lower alkyl-amino, di-lower alkylamino, piperazinyl, piperidinyl, pyrrolidinyl or by morpholinyl, or lower alkanoyl, trifluoromethyl, hydroxy, lower alkoxy, lower alkanoyloxy, halogen, amino, lower alkylamino, di-lower alkylamino, lower alkanoylamino, benzoylamino, carboxy or lower alkoxycarbonyl,  
or a salt of such a compound having at least one salt-forming group.

4. A compound of formula I according to claim 1, wherein

R<sub>1</sub> is pyridyl bonded at a ring carbon atom and unsubstituted or substituted at the nitrogen atom by oxygen,  
R<sub>2</sub> and R<sub>3</sub> are each hydrogen,  
R<sub>4</sub> is hydrogen or lower alkyl,  
R<sub>5</sub> is hydrogen, lower alkyl or fluoro-substituted lower alkoxy,  
R<sub>6</sub> is hydrogen,  
R<sub>7</sub> is nitro, fluoro-substituted lower alkoxy or a radical of formula II wherein  
R<sub>9</sub> is hydrogen,  
X is oxo,  
n is 0 and  
R<sub>10</sub> is an aliphatic hydrocarbon radical having 5-22 carbon atoms, a phenyl radical that is unsubstituted or substituted by cyano, lower alkyl, (4-methyl-piperazinyl)-lower

alkyl, lower alkoxy, halogen or by carboxy; a cycloalkyl radical having up to 30 carbon atoms or a monocyclic radical having 5 or 6 ring members and 1-3 sulfur ring atoms, and

R<sub>8</sub> is hydrogen,

or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

5. A compound of formula I according to claim 1, wherein

R<sub>1</sub> is pyridyl or N-oxido-pyridyl each of which is bonded at a carbon atom,

R<sub>2</sub> and R<sub>3</sub> are each hydrogen,

R<sub>4</sub> is hydrogen or lower alkyl,

R<sub>5</sub> is hydrogen, lower alkyl or trifluoromethyl,

R<sub>6</sub> is hydrogen,

R<sub>7</sub> is nitro, fluoro-substituted lower alkoxy or a radical of formula II wherein

R<sub>9</sub> is hydrogen,

X is oxo,

n is the number 0 and

R<sub>10</sub> is pyridyl bonded at a carbon atom, phenyl that is unsubstituted or substituted by halogen, cyano, lower alkoxy, carboxy, lower alkyl or by 4-methyl-piperazinyl-methyl, or C<sub>5</sub>-C<sub>7</sub>alkyl, thienyl, 2-naphthyl or cyclohexyl, and

R<sub>8</sub> is hydrogen,

or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

6. A compound according to claim 1 of formula I, wherein R<sub>4</sub> and R<sub>8</sub> are each hydrogen and the remaining substituents are as defined in claim 1, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

7. A compound according to claim 3 of formula I, wherein R<sub>4</sub> and R<sub>8</sub> are each hydrogen and the remaining substituents are as defined in claim 3, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

8. A compound according to claim 4 of formula I, wherein R<sub>4</sub> and R<sub>8</sub> are each hydrogen and the remaining substituents are as defined in claim 4, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

9. A compound according to claim 5 of formula I, wherein  $R_4$  and  $R_8$  are each hydrogen and the remaining substituents are as defined in claim 5, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

10. A compound according to claim 1 of formula I, wherein at least one of the radicals  $R_4$  and  $R_8$  is lower alkyl, and the remaining substituents are as defined in claim 1, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

11. A compound according to claim 3 of formula I, wherein at least one of the radicals  $R_4$  and  $R_8$  is lower alkyl, and the remaining substituents are as defined in claim 3, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

12. A compound according to claim 4 of formula I, wherein at least one of the radicals  $R_4$  and  $R_8$  is lower alkyl, and the remaining substituents are as defined in claim 4, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

13. A compound according to claim 5 of formula I, wherein at least one of the radicals  $R_4$  and  $R_8$  is lower alkyl, and the remaining substituents are as defined in claim 5, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

14. A compound according to claim 1 of formula I, wherein  
 $R_1$  is pyridyl bonded at a carbon atom,  
 $R_2, R_3, R_4, R_5, R_6$  and  $R_8$  are each hydrogen and  
 $R_7$  is nitro or a radical of formula II wherein  
 $R_9$  is hydrogen,  
 $X$  is oxo,  
 $n$  is the number 0 and  
 $R_{10}$  is pyridyl bonded at a carbon atom, phenyl that is unsubstituted or substituted by fluorine, chlorine, cyano, lower alkoxy, carboxy, lower alkyl or by 4-methyl-piperazinyl-methyl, or  $C_5$ - $C_7$ alkyl, thienyl or cyclohexyl,  
or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 1 of formula I, wherein R<sub>1</sub> is 4-pyridyl, N-oxido-4-pyridyl, 3-indolyl, and R<sub>7</sub> is fluoro-substituted alkoxy containing up to 2 carbon atoms, or a salt of such a compound containing at least one salt-forming group.

16. A compound of formula I according to claim 1, wherein R<sub>1</sub> is 4-pyridyl, N-oxido-4-pyridyl, 3-indolyl, and R<sub>7</sub> is trifluoromethoxy or 1,1,2,2-tetrafluoroethoxy, or a salt of such a compound containing at least one salt-forming group.

17. N-(5-Benzoylamido-2-methyl-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine or a pharmaceutically acceptable salt thereof according to claim 1.

18. N-[3-(1,1,2,2-Tetrafluoroethoxy)phenyl]-4-(4-pyridyl)-2-pyrimidine-amine or a pharmaceutically acceptable salt thereof according to claim 1.

19. A compound according to claim 1 of the formula I or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group selected from N-(3-Nitro-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Chlorobenzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Benzoylamido-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(2-Pyridyl)carboxamido-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(3-Pyridyl)carboxamido-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Pyridyl)-carboxamido-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Pentafluoro-benzoylamido-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(2-Carboxy-benzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-n-Hexanoylamido-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Nitro-phenyl)-4-(2-pyridyl)-2-pyrimidine-amine, N-(3-Nitro-phenyl)-4-(4-pyridyl)-2-pyrimidine-amine, N-[3-(2-Methoxy-benzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Fluoro-benzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Cyano-benzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(2-Thienylcarboxamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Cyclohexylcarboxamido-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Methyl-benzoylamido)-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[3-(4-Chloro-benzoylamido)-phenyl]-4-(4-pyridyl)-2-pyrimidine-amine, N-[3-[4-(4-Methyl-piperazino-methyl)-benzoylamido]-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[5-[4-(4-Methyl-piperazino-methyl)-benzoylamido]-2-methyl-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[5-(4-Methyl-benzoylamido)-2-methyl-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[5-(2-Naphthoylamido)-2-methyl-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[5-(4-Chloro-benzoylamido)-2-methyl-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-[5-(2-

*put in context*

Methoxy-benzoylamido)-2-methyl-phenyl]-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Tri-fluoromethoxy-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-[1,1,2,2-Tetrafluoro-ethoxy]-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Nitro-5-methyl-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Nitro-5-trifluoromethyl-phenyl)-4-(3-pyridyl)-2-pyrimidine-amine, N-(3-Nitro-phenyl)-4-(N-oxido-3-pyridyl)-2-pyrimidine-amine, N-(3-Benzoylamido-5-methyl-phenyl)-4-(N-oxido-3-pyridyl)-2-pyrimidine-amine and the pharmaceutically acceptable salts of such a compound having at least one salt-forming group.

20. A compound according to claim 1 of the formula I or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group selected from N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-4-(N-oxido-4-pyridyl)-2-pyrimidine-amine and N-[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-4-(3-indolyl)-2-pyrimidine-amine and the pharmaceutically acceptable salts of such a compound having at least one salt-forming group.

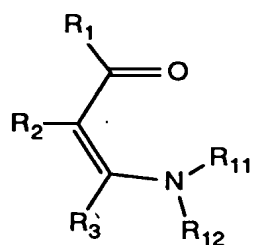
21. A pharmaceutical composition for the treatment of tumours in warm-blooded animals including humans, comprising, in a dose effective against tumours, a compound of formula I according to claim 1, or a pharmaceutically acceptable salt of such a compound having at least one salt-forming group, together with a pharmaceutical carrier.

22. A method of treating warm-blooded animals including humans, which comprises administering to such a warm-blooded animal suffering from a tumoral disease a dose, effective against tumours, of a compound of formula I according to claim 1 or of a pharmaceutically acceptable salt of such a compound having at least one salt-forming group.

23. A process for the preparation of a compound of formula I according to claim 1 or of a salt of such a compound having at least one salt-forming group, which comprises

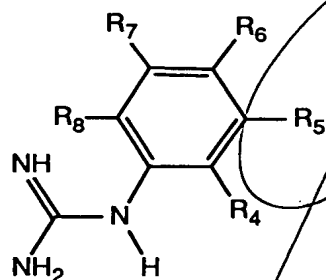
a) reacting a compound of formula III

*50*



(III),

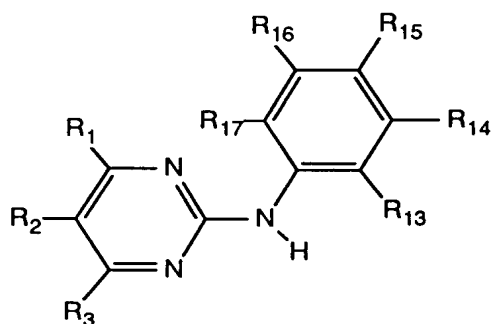
wherein R<sub>11</sub> and R<sub>12</sub> are each independently of the other lower alkyl and R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are as defined above, functional groups present in a compound of formula III, with the exception of the groups participating in the reaction, being if necessary in protected form, or a salt of such a compound, with a compound of formula IV



(IV),

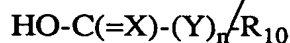
wherein the substituents are as defined above, functional groups present in a compound of formula IV, with the exception of the guanidino group participating in the reaction, being if necessary in protected form, or with a salt of such a compound, and removing any protecting groups present, or

b) for the preparation of a compound of formula I wherein the radicals R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are as defined above with the exception of nitro and fluoro-substituted lower alkoxy, reacting a compound of formula V



(V),

wherein one or two of the radicals R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are each amino and the remaining radicals R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, R<sub>16</sub> and R<sub>17</sub> are each independently of the others hydrogen, lower alkyl that is unsubstituted or substituted by free or alkylated amino, piperazinyl, piperidinyl, pyrrolidinyl or by morpholinyl, or lower alkanoyl, trifluoromethyl, free, etherified or esterified hydroxy, free, alkylated or acylated amino or free or esterified carboxy, and the remaining substituents are as defined above, functional groups present in a compound of formula V, with the exception of the amino group(s) participating in the reaction, being if necessary in protected form, with a compound of formula VI



(VI),

wherein the substituents and symbols are as defined above, functional groups present in a compound of formula VI, with the exception of the HO-C(=X) group participating in the reaction, being if necessary in protected form, or with a reactive derivative of a compound of formula VI, and removing any protecting groups present, or

c) for the preparation of a compound of formula I wherein R<sub>1</sub> is pyridyl substituted at the nitrogen atom by oxygen, and wherein the other substituents and symbols are as defined above, converting a compound of formula I wherein R<sub>1</sub> is pyridyl into the N-oxido compound with a suitable oxidising agent, and, if desired, converting a compound of formula I obtainable by any one of processes a to c into its salt, or converting an obtainable salt of a compound of formula I into the free compound.

add  
a<sub>3</sub>